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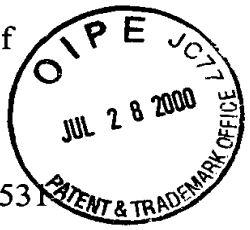
Patent
Attorney's Docket No. 016800-111

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**




In re Patent Application of )
)
Yann MAHE et al ) Group Art Unit: 1642
)
Application No.: 08/716,531 ) Examiner: S. Huff
)
Filed: September 19, 1996 ) Appeal No. Unassigned
)
For: PHARMACEUTICAL/COSMETIC )
COMPOSITIONS COMPRISING )
THE LYSINE-D-PROLINE- )
VALINE TRIPEPTIDE )

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8-2-00



**BRIEF FOR APPELLANT**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This appeal is from the decision of the Primary Examiner dated December 8, 1999 (Paper No. 27), which decision was maintained in the Advisory Action dated May 16, 2000 (Paper No. 30), finally rejecting Claims 1 through 11 and 16 through 19 based on prior art grounds, which are reproduced as an Appendix to this brief.

The rejections for purposes of this Appeal are as follows:

(i) Claims 1 to 3 stand rejected under 35 U.S.C. §102(b) as being anticipated by Ferreira et al, U.S. Patent 5,389,615, or Oluyomi et al, *Eur. J. Pharm.* 258:131 (1994.)

(ii) Claims 4, 7 to 10 and 18 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ferreira et al, USP 5,389,615.

(iii) Claims 5, 6 and 19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ferreira et al, USP 5,389,615, in view of Lipton, USP 5,157,023 and Oluyomi et al, *Eur. J. Pharm.*, 258:131 (1994.)

(iv) Claims 1 to 11 and 16 to 19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ferreira et al, USP 5,389,615, in view of Norlund et al, USP 4,874,744, Lipton, USP 5,157,023, and *Remington's Pharmaceutical Sciences*, 16th Ed (1980), Chapters 87 and 92, and Oluyomi et al, *Eur. J. Pharm.*, 258:131(1994.)

(v) Claims 1 to 3, 5 to 11 and 16 to 19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Oluyomi et al, *Eur. J. Pharm.* 258:131 (1994), in view of Norlund et al, USP 4,874,744, Lipton, USP 5,157,023, and *Remington's Pharmaceutical Sciences*, 16th Ed. (1980), Chapters 87 and 92.

The Government fee of [X] $300.00 (120) is to be charged to Deposit Account 02-4800. **Two extra copies of this Brief are being filed herewith.**

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in triplicate.

**Real Party in Interest**

The present application is assigned to SOCIÉTÉ L'ORÉAL S.A., a corporation of France.

## I. Related Appeals and Interferences

The Appellants' legal representative, or Assignee does not know of any other appeal or interferences which will affect or be directly affected by or have bearing on the Board's decision in the pending appeal.

## II. Status of Claims

Claims 1 through 11 and 16 through 19 are pending. All of these claims are subject to appeal.

## III. Status of Amendments

Three Amendments were submitted during prosecution of this application, on July 10, 1997, January 15, 1998, and March 13, 1998, each of which amendments were entered in their entirety.



## IV. Summary of the Invention

The invention as set forth in the claims under Appeal relates to a method of treating inflammation comprising administering a therapeutically effective amount of a pharmaceutical/cosmetic composition of matter, comprising an anti-inflammatory effective amount of a peptide comprising the lysine-proline-valine tripeptide sequence, wherein the proline moiety exists in its dextrorotatory optical isomer form (DPro), and the lysine and valine residues can exist either in their levorotatory or dextrorotatory optical forms.

In preferred embodiments, the tripeptide will comprise D-Lys-D-Pro-D-Val, D-Lys-D-Pro-L-V-1, L-Lys-D-Pro-D-Val or L-Lys-D-Pro-L-Val, and may further include protecting groups to enhance stability. A composition containing such tripeptide will preferably be topically applied to the skin, scalp and/or mucous membranes of a mammalian organism in order to alleviate inflammation.

In other preferred embodiments, as set forth in Claims 18 and 19, respectively, the peptide will be administered in combination with other anti-inflammatory agents, and will preferably contain a protecting group at the C-terminal end.

It was unexpected, based on the state of the prior art, that the subject peptide would exhibit anti-inflammatory activity.

As discussed at page 3 of the subject application, while it had been previously proposed to administer derivatives of α-type melanocyte-stimulating hormone ((α-MSH) or melanotropin and specifically a peptide containing lysine-proline-valine to treat inflammation (US Patents 5,028,592 and 5,157,023), the previous anti-inflammatory peptides contained proline in its conventional levorotatory form. In fact, it was previously reported in the literature, that if the proline residue existed in its dextrorotatory rather than levorotatory form, that the tripeptide lost all effectiveness for the treatment of inflammation. (Hiltz et al, *Peptides*, 12:767-771 (1991.)) Therefore, it was an entirely unexpected discovery made by the present Appellants that a peptide containing the Lys-Pro-Val tripeptide, wherein the proline residue is in its dextrorotatory form, exhibits

potent anti-inflammatory activity. The anti-inflammatory activity of the subject peptide is evidenced by the results contained in the subject application, especially Examples 1 through 4, which substantiate that the subject peptide inhibits inflammatory and pro-inflammatory cytokines (IL-1α, IL-1R1, IL-1R2), and that this activity is comparable to tripeptides containing the natural (L)-Pro form.

## V. The Issues

The issue is whether the prior art cited by the Examiner anticipates or renders obvious the claimed methods of inhibiting inflammation by administration of an effective (anti-inflammatory amount) of a peptide containing the tripeptide lysine-proline-valine, wherein the proline moiety is in its dextrorotatory form.

## VI. Grouping of Claims

Claims 1 to 11 and 16 to 19 are subject to this Appeal. Claim 1 is the only independent claim. While all the claims are believed to be separately patentable, only the patentability of Claim 19, which provides for the administered peptide to be acidyl-(D) Lys-(D) Pro-(D) Val-$NH_2$ or acidyl-(L) Lys-(D) Pro-(L) Val-$NH_2$ is separately argued.

## VII. Argument

### A. The Cited References

#### 1. Ferreira et al, US Patent 5,389,615

Ferreira et al relates to peptides and pharmaceutical compositions useful for the treatment of pain. These peptides include Lys-Pro-Thr, Lys-D-Pro-Thr, Lys-Pro-Val, and

Lys-D-Pro-Val. However, the reference does not teach that such peptides inhibit inflammation, only that they effectively treat pain. This pain includes that triggered by inflammatory agents.

**2. Oluyomi et al, *Eur. J. Pharm.* 258:131 (1994)**

Oluyomi et al describes the anti-nociceptive (anti-pain) activity of peptides related to interleukin. The reference describes in particular that various peptides, including Lys-D-Pro-Val, effectively inhibit pain which includes pain associated with inflammation. However, the reference clearly states that the presence of the L-$Pro_{12}$ (levorotatory form of amino acid) of α-MSH "is thought to be important in the anti-inflammatory response to picryl chloride injection (Hiltz et al, 1991), as Lys-D-Pro-Thr was found to be ineffective on swelling, a major characteristic of inflammation" (*see* page 137, left-hand column of reference). Oluyomi et al (*Id.*) also discloses that "Hiltz et al (1991), however, found that altering the stereochemical make-up of their tripeptides via D-substitution with D-amino acids increased stability, potency and duration of activity but [resulted in] loss of anti-inflammatory activity (underlined for emphasis.) (See p. 137, left-hand column, lines 27-35.)

**3. Lipton U.S. Patent No. 5,389,615**

Lipton discloses the use of peptides containing the amino acid sequence lysine-proline-valine for reduction of fever and inflammation. The tripeptide is either isolated from natural sources or is synthesized, and may comprise protecting groups at its carboxy

and/or amino terminus. Lipton, however, fails to teach or suggest peptides containing proline in its dextrorotatory form. Rather, the listed peptides contain naturally-occurring optical amino acids (levorotatory forms.)

**4. Norlund et al, U.S. Patent No. 4,874,744**

This reference describes treatment of dermatitis and inflammation by topical application of a composition containing melanocyte-stimulating hormone to the skin. The reference does not teach the use of Lys-D(Pro)-Val to inhibit anti-inflammation.

**5. *Remington's Pharmaceutical Sciences***

This reference is cited based on its disclosure relating to topically administrable formulations and aerosols, including ointments and creams.

**B. The Examiner's Rationale**

The Examiner's rationale, as set forth in the final rejection mailed December 28, 1999, is as follows:

> Claims 1-3 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ferreira et al US 5389615 or Oluyomi et al Eur. J. Pharm. vol. 258 p. 131 (1994.)
>
> Claims 4, 7-10 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Ferreira et al US 5389615 as applied to claims 1-3 above.
>
> Claims 5-6 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Ferreira et al US 5389615 as applied to claims 1-3 above further in view of Lipton US 5157023 and Oluyomi et al Eur. J. Pharm. vol. 258 p. 131 (1994.)

> Claims 1-11 and 16-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over by Ferreira et al US 5389615 in view of Norlund et al US 4874744, Lipton US 5157023 and Remington's Pharmaceutical Sciences, 16th ed. (1980), Ch. 87 and 92 and Oluyomi et al Eur. J. Pharm. vol. 258 p. 131 (1994.)
>
> Claims 1-3, 5-11 and 16-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Oluyomi et al Eur. J. Pharm. vol. 258 p. 131 (1994) in view of Norlund et al US 4874744, Lipton US 5157023 and Remington's Pharmaceutical Sciences, 16th ed. (1980), Ch. 87 and 92.

Essentially, the Examiner's rationale in all these rejections is that the prior art purportedly teaches or suggests the use of a peptide containing the tripeptide Lys-D-Pro-Val to inhibit inflammation. Based on the following, Appellants respectfully disagree.

**1. The Anticipatory Rejection of Claims 1-3 Based on Ferreira et al, U.S. Patent 5,389,615 Should Be Reversed as it is Improper**

The rejection based on Ferreira et al should be reversed as the reference fails to teach the claimed method of administering a peptide containing Lys-D-Pro-Val for treating inflammation. Rather, the reference is limited in its teachings to the use of a specific related class of peptides which includes Lys-D-Pro-Val for treating pain. This is clear, e.g., from the Abstract and claims of the patent. There is absolutely no indication in the reference that the peptide could be used to treat inflammation as claimed.

The Examiner improperly concluded during prosecution that treating pain is equivalent to treating inflammation (particularly because Ferreira et al describes that the

pain which is treated includes pain elicited by inflammatory agents.) However, this is respectfully submitted to be improper.

This conclusion is improper as inflammation and pain are not equivalent. Further Appellants respectfully submit that this rejection is improper as it cannot be reasonably extrapolated that a compound which is suitable for treating pain would be suitable for treating inflammation. These arguments are supported by a Declaration of record, i.e., of Yann Mahe, an expert in the art, having particular expertise in the area of inflammation and pro-inflammatory cytokines. In particular, the Board is respectfully referred to paragraph (12) of this Declaration, wherein Dr. Mahe states that in his expert opinion it is not reasonably predictable that a compound which inhibits pain will inhibit inflammation. Based thereon, it is wholly improper to reasonably expect, absent any scientific support, that a compound which inhibits pain, even pain associated with inflammation, would have any significant effect on inflammation. Indeed, these are different processes which cannot predictably be treated using the same active agents.

In this regard, the Board is also respectfully referred to Appellants' January 15, 1998 Reply, wherein Appellants cited pages from a textbook substantiating that drugs for suppressing inflammatory and immune reactions are often distinct from compounds used for treating analgesia, i.e., pain. For example, this Reply made reference to the paracetamol compound which, while possessing the ability to inhibit pain and to exhibit antipyretic effects, exhibits absolutely no anti-inflammatory activity. This is because

inflammation is a distinct phenomena from pain, notwithstanding the fact that inflammation may sometimes be associated with pain.

As yet, additional evidence of the well-known fact in the pharmacological art that pain cannot be equated with inflammation and, moreover, that it cannot be reasonably extrapolated that a compound which inhibits pain would have a similar effect on inflammation, Appellants refer to the Abstract by Hoffman and Schmelz from the Eur. *J. Pain*, 1999 3(2):131-139 submitted during prosecution of this application. This Abstract contains evidence substantiating that the time course of hyperalgesia (pain) and erythema in human skin (following UVA and UVB radiation) are distinct from inflammation. The authors note that these phenomena have different time courses, i.e., erythema and hyperalgesia exhibit a typical time course, which differs from inflammation. In fact, the Abstract makes clear that the inflammatory mediators responsible for vasodilation are not the same as those for inducing hyperalgesia and that hyperalgesia is elicited by different stimuli than inflammatory mediators which result in inflammation. Therefore, this reference provides further evidence substantiating that inflammation and pain are different phenomena which are triggered by different mechanisms. This supports Appellants' arguments that it would not have been reasonably predicted that a compound which inhibits pain would have any demonstrable effect on inflammation as these are very different phenomena.

The Examiner also maintained the anticipatory rejection because of her misplaced conclusion that a method for treating inflammation would "overlap" with a method for treating pain. However, this conclusion cannot be substantiated upon a complete understanding of inflammation *vis-a-vis* pain. Inflammation is a very complex phenomena which is described at pages 1-2 of the subject application. Specifically, inflammation involves a set of biological reactions which involve a series of non-specific reactions which are triggered by various phenomena that are initiated by various stimuli that result in three phenomena, i.e., vascular, cellulovascular and tissue fibrosis. Localized inflammation is associated with swelling, pain, redness, and warmth. Also, inflammation is generally attributable to the infiltration of injured tissues by an edema or vasodilation of capillaries. Therefore, inflammation, while it may be associated with pain, has a very complex physiology and is not equivalent to pain. In fact, inflammation is mediated by a variety of different factors, including cytokines, chemotactic factors, as well as other factors involved in the inflammatory cascade, such as aracadonic acid, prostaglandin, and other compounds. Based on the complex physiology and elicitors of inflammation, Appellants respectfully submit that the Examiner's conclusion that one of ordinary skill would reasonably conclude that a method of treating pain would correlate to a method for treating inflammation is wrong. This is simply not the case.

Based thereon, reversal of the anticipatory rejection of Claims 1 to 3 based on Ferreira et al, USP 5,389,615, is respectfully requested.

**2. The Anticipatory Rejection of Claims 1-3 Based on Oluyomi (*Eur. J. Pharm.*, 258:131 (1999)) Should Be Reversed as it is Improper**

Oluyomi et al also fails to anticipate or render obvious the subject invention. As argued during prosecution, Oluyomi in fact teaches against the claimed invention as it suggests that for anti-inflammatory peptides containing the tripeptide Lys-Pro-Val, the levorotatory form of proline is essential for anti-inflammatory activity. This appraisal of the reference is supported by the fact that the authors refer substantially to an earlier article by Hiltz et al, *Peptides*, 12:767-771 (1990). Upon review of the reference, it is quite clear that Oluyomi et al in their 1994 publication gave considerable weight to an earlier Hiltz et al article, since they base many of their conclusions on this reference. Therefore, even in 1994, i.e., three years later, these results were still regarded to be significant.

More specifically, for the reasons argued during prosecution of this application, Hiltz et al clearly teaches against the subject invention since it is quite clear that the authors of this reference were of the opinion that the levorotatory form of proline in the Lys-Pro-Val sequence is significant (essential) to its anti-inflammatory activity. For example, in the results section at page 769, Hiltz et al indicates that a peptide comprising the dextrorotatory form of proline "had no significant effect on inflammation". Moreover, in the discussion section of the reference, when they summarize their conclusions, they state the following: "This finding underlines again the importance of L-Pro to the anti-

inflammatory responses." Still further, at page 770, right-hand column, the authors refer to the fact that the loss of activity (anti-inflammatory activity) with D-Pro$^{12}$ substitution has been described previously. Therefore, contrary to the position taken by the Examiner during prosecution, Hiltz et al are not ambiguous in their conclusions as to the lack of anti-inflammatory activity of the subject peptides or the essentiality of the L-Pro residue to anti-inflammatory activity. To the contrary, the authors expressed their opinion unequivocably that L-Pro is critical to the anti-inflammatory activity of the studied peptides.

With respect to such argument, the Examiner alleged during prosecution that it is not clear which phase of inflammation Hiltz et al is referring to when they say it is inactive. However, the Examiner's position is unsustainable. Indeed, based on the express statements excerpted above, the authors are unambiguous in their conclusions, i.e., the fact that L-Pro is significant for anti-inflammatory activity. They do not equivocate their conclusions and do not suggest that their results are dependent upon the particular phase of inflammation.

Rather, a fair and reasonable assessment of Oluyomi is that the reference is primarily directed to evaluation of the anti-nociceptive activity of peptides related to interleukin-1β, i.e., and the use of such peptides for treating pain (anti-analgesic). This activity is evaluated in tests conventionally used to elicit pain as described at page 132 of the reference. These tests include, in particular, the rat paw test. Based on the results,

the authors note that the disclosed peptides, which include Lys-D-Pro-Val $NH_2$ may represent peripherally acting analgesic compounds. They further note that such peptide is only active in the late phase of formalin-induced nociceptive response and that such peptide is relatively less potent in comparison to peptides in a first group (see page 137, right-hand column of the reference). Based thereon, they suggest that the peptides studied in the reference may be useful for inhibition of pain. They do not suggest the anti-inflammatory activity of the subject tripeptide.

During prosecution, the Examiner alleged, based on the statement at page 137, left-hand column, lines 1-6, of Oluyomi, that the use of the subject peptide to that inflammation could have been obvious or anticipated. Therein, Oluyomi states as follows: "the peripheral anti-inflammatory activity of this peptide as reported by Hiltz and Lipton (1989) and its analogs (Hiltz et al, 1991)." However, as stated in the §132 Declaration of record, Hiltz et al does not teach or suggest the anti-inflammatory activity of the subject peptide. Indeed, the reference teaches exactly the reverse. Therefore, one of ordinary skill, reading this reference together with the references and earlier scientific data on from which they base their conclusions, would reasonably conclude that the subject peptide would not elicit anti-inflammatory activity because it contains the dextrorotatory form of proline. Also, one of ordinary skill, reading the Oluyomi et al reference, would be expected to read the reference in its entirety. For example, the very next paragraph refers to the same 1991 Hiltz et al reference and they state as follows:

"L-Pro$^{12}$ of α-MSH is though to be important in the anti-inflammatory response." Also, as stated above, the authors further go on to state that alteration of the disclosed tripeptides via D-substitution while increasing stability and potency and duration of action (anti-nociceptive activity) results in loss of anti-inflammatory activity. Therefore, Appellants respectfully submit that the reference does not reasonably suggest the subject invention. To the contrary, the reference is directed to the study of various peptides, includes Lys-Pro-Val, for inhibition of pain. However, the reference does not fairly suggest the use of lysine-D-proline-valine for inhibiting inflammation as claimed herein.

Reversal of the anticipatory rejection of Claims 1 to 3 based on Oluyami et al is therefore respectfully requested.

### 3. The Rejection of Claims 4, 7-10 and 18 under 35 U.S.C. §103 As Being Obvious Over Ferreira et al Should Be Reversed as it is Improper

The Ferreira reference has been discussed above in the rebuttal of the anticipatory rejection of Claim 3. For the reasons set forth therein, the reference describes the analgesic (anti-pain) activity of various peptides, including those containing lysine-proline-valine. The reference does not teach or suggest the use of such peptides for inhibiting inflammation as claimed. Also, for the reasons of record, which are supported by the Declaration of Yann Mahe, dated July 20, 1998, inflammation and pain cannot be equated. Withdrawal of this rejection is therefore respectfully requested.

**4. The Rejection of Claims 5, 6 and 19 under 35 U.S.C. §103 As Assertedly Being Unpatentable Over The Combination of Ferreira et al In View of Lipton and Oluyomi et al Should be Reversed As it is Improper**

Ferreira et al has been discussed above, as has Oluyomi et al. For the reasons set forth therein, these references, separately or in combination, fail to teach or suggest the invention. To the contrary, they merely relate to the use of various peptides for inhibition of pain. However, they do not teach or suggest the activity of the subject tripeptide as an anti-inflammatory agent. In fact, such activity is unexpected based on prior art references discussed in the Oluyomi et al reference, which would have reasonably suggested the contrary. As discussed above, the accepted view in the prior art, prior to the present invention was that for peptides containing the tripeptide lys-pro-val, that the L(Pro) was essential for anti-inflammatory activity.

The deficiencies of Ferreira and Oluyomi et al are not cured by Lipton. This reference also does not teach or suggest the anti-inflammatory activity of the subject tripeptide, i.e., Lys-Pro-Val, wherein proline is in its dextrorotatory form. Rather, the reference relates to peptides which are in their conventional L-form and protected versions of such peptides for reducing fever and inflammation. Therefore, based on the foregoing, withdrawal of the §103 rejection of Claims 5, 6 and 19 based on Ferreira et al in view of Lipton and Oluyomi et al is respectfully requested.

**5. The Rejection of Claims 1-11 and 16-19 under 35 U.S.C. §103 As Being Unpatentable Over Ferreira et al In View of Norlund et al, Lipton and Remington's Pharmaceutical Sciences, and Oluyomi et al Should Be Reversed.**

The Ferreira et al, Lipton, and Oluyomi et al references have been discussed above. For the reasons set forth therein, these references fail to teach or suggest the anti-inflammatory activity of the tripeptide lys-pro-val sequence which contains proline in its dextrorotatory form. The deficiencies of the rejection are further not cured by Remington's Pharmaceutical Sciences and Norlund et al.

Norlund et al relates to the treatment of dermatitis by topical application of a composition including a melanocyte-stimulating hormone. However, the reference fails to teach or suggest the anti-inflammatory activity of the specific tripeptide, i.e., Lys-Pro-Val, wherein Pro is in its dextrorotatory form.

Similarly, Remington's Pharmaceutical Sciences fails to teach or suggest the anti-inflammatory activity of the subject peptide. In fact, Remington's was cited merely based on its discussion relating to various pharmaceutical compositions and modes of administration including typically administrable forms. Therefore, the cited combination of references also fails to teach or suggest the invention since there is nothing which would allow one to reasonably infer the anti-inflammatory activity of the subject tripeptide. Withdrawal of the §103 rejection of Claims 1-11 and 16-19 based on Ferreira

et al, in view of Norlund et al, Lipton, Remington's Pharmaceutical Sciences, and Oluyomi et al is therefore respectfully requested.

6. **The Rejection of Claims 1-3, 5-11 and 16-19 under 35 U.S.C. §103 As Being Unpatentable Over Oluyomi et al (1994) In View of Norlund et al, Lipton and Remington's Pharmaceutical Sciences Should Be Reversed as it is Improper.**

All of these references have been discussed above. For the reasons already enumerated, the references, separately or in combination, fail to teach or suggest the anti-inflammatory activity of the subject peptide. Rather, the references merely suggest the anti-nociceptive, i.e., analgesic, activity of the subject tripeptide. The only references which relate to inhibiting inflammation do not teach or suggest the anti-inflammatory activity of the specific tripeptide of the invention (Oluyomi) since the reference expressly indicates that the D-Pro residue is essential for anti-inflammatory activity. By contrast, it has been surprisingly discovered, based on the results contained in the subject application, that the subject tripeptide, Lys-Pro-Val, wherein the proline is in its dextrorotatory form, exhibits substantially the same activity as the tripeptide lys-pro-val wherein the proline is in its levorotary form.

Therefore, as these results are unexpected, reversal of the §103 rejection of Claims 1 to 3, 5 to 11 and 16 to 19 based on Oluyami et al in view of Norlund, Lipton et al and Remington's is respectfully requested.

## VIII. Conclusion

In conclusion, all the prior art rejections should be reversed because the prior art alone or in combination fails to teach or suggest that a peptide comprising lys-D-pro-val would inhibit inflammation. Rather, the prior art only suggests the antinociceptive (anti-pain) activity of this peptide and actually teaches against its use as an anti-inflammatory given the prior belief as to the essentiality of the L form of proline on inflammatory activity.

Respectfully submitted,

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APPENDIX



**The Appealed Claims**

1. A method of treating inflammation comprising administering a therapeutically effective amount of a pharmaceutical/cosmetic composition of matter, comprising an anti-inflammatory effective amount of at least one peptide comprising the lysine-proline-valine tripeptide sequence, the proline moiety of which exists in its dextrorotatory optical isomer form (DPro), wherein said peptide comprises anti-inflammatory activity, in a physiologically/pharmaceutically acceptable medium therefor, and where the lysine and valine residues contained in said lysine-proline-valine tripeptide sequence exist either in their levorotatory of dextrorotary forms.

2. The method as defined in Claim 1, said tripeptide sequence comprising the last three amino acids situated at the C-terminal end of said at least one peptide.

3. The method as defined in Claim 1, said at least one peptide comprising the lysine-proline-valine tripeptide, the proline moiety of which exists in its dextrorotary optical isomer form (DPro).

4. The method as defined in Claim 1, said at least one peptide comprising the lysine-proline-valine tripeptide, the lysine, proline and valine moieties of which exist in their dextrorotatory optical isomer forms (D-Lys-D-Pro-D-Val).

5. The method as defined in Claim 1, said at least one peptide including at least one protective group situated at the C-terminal and/or N-terminal end of said peptide.

6. The method as defined in Claim 5, wherein said at least one protective group [wherein said composition] (sic) comprises an acyl, acetyl and/or amido group.

7. The method as defined in Claim 1, wherein said composition comprises from $10^{-12}$M to $10^{-3}$M of said tripeptide sequence.

8. The method as defined in Claim 7, wherein said composition comprises from $10^{-9}$M to $10^{-4}$M of said tripeptide sequence.

9. The method as defined in Claim 1, wherein said composition comprises from $10^{-12}$M to 1M of said tripeptide sequence.

10. The method as defined in Claim 9, wherein said composition comprises from $10^{-6}$M to $10^{-1}$M of said tripeptide sequence.

11. The method as defined in Claim 1, wherein said composition comprises a lotion, gel, milk, serum, cream, sunscreen, emulsion, shampoo, dentifrice, ointment, aerosol or spray.

16. The method according to Claim 1, wherein the pharmaceutical/cosmetic composition is topically applied.

17. The method according to Claim 1, wherein the pharmaceutical/cosmetic composition is topically applied to the skin, scalp and/or mucous membrane of a mammalian organism.

18. The method according to Claim 1, wherein the pharmaceutical/cosmetic composition which is administered further comprises an effective anti-inflammatory amount of at least one glucocorticoid, vitamin D or derivative thereof, and/or non-steroidal anti-inflammatory agent.

19. The method according to Claim 1, wherein said lysine-proline-valine tripeptide sequence contained in said pharmaceutical/cosmetic composition is acidyl-(D) Lys-(D) Pro-(D) Val-$NH_2$ or acidyl-(L) Lys-(D) Pro-(L) Val-$NH_2$.

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